

CLAIMS

1. An (S)-secondary alcohol of formula (VIII A)



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where:

(I) R_N is C_1-C_5 alkyl;

(II) X_2 is:

(A) -Cl,

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(B) -Br,

(C) $p-CH_3-\phi-SO_2-$,

(D) $m-NO_2-\phi-SO_2-$.

2. An (S)-secondary alcohol (VIII A) according to claim 1 where R_N is C_1 alkyl.

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3. An (S)-secondary alcohol (VIII A) according to claim 1 where X_2 is -Cl.

4. An (S)-secondary alcohol (VIII A) according to claim 1 which is selected from the group consisting of (S)-1-acetamido-2-hydroxy-3-chloropropane.

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5. An (S)-epoxide of formula (VIII B)



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where:

(I) where R_N is C_1-C_5 alkyl;

(II) where # indicates that the atoms marked with a (#) are bonded to each other resulting in the formation of a ring.

- 30 6. An (S)-epoxide (VIII B) according to claim 5 where R_N is C_1 alkyl.

7. An (S)-epoxide (VIII B) according to claim 5 which is selected from the group consisting of (S)-glycidylacetamide.

- 35 8. An (S)-ester of formula (VIII C)



where:

(I) where R_N is C_1-C_5 alkyl;

5 (II) where X_2 is:

(A) -Cl,

(B) -Br,

(C) $p-CH_3-\phi-SO_2-$,

(D) $m-NO_2-\phi-SO_2-$.

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9. An (S)-ester (VIII C) according to claim 8 where R_N is C_1 alkyl.

10. An (S)-ester (VIII C) according to claim 8 where X_2 is -Cl.

15 11. An (S)-epoxide (VIII C) according to claim 8 which is (S)-1-acetamido-2-acetoxy-3-chloropropane.

12. A compound selected from the group consisting of:

(1) an (S)-protected alcohol of the formula (IV A)

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where:

(I) X_0 is:

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(A) - ϕ ,

(B) *o*-hydroxyphenyl,

(C) *o*-methoxyphenyl,

(D) *p*-methoxyphenyl;

(II) X_2 is:

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(A) -Cl,

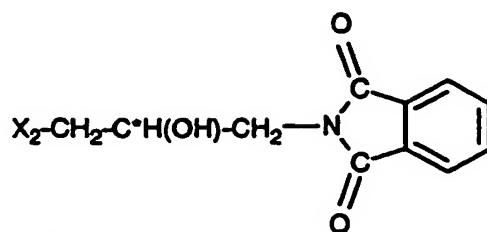
(B) -Br,

(C) $p-CH_3-\phi-SO_2-$,

(D) $m-NO_2-\phi-SO_2-$;

(2) an (S)-phthalimide alcohol of the formula (IVC)

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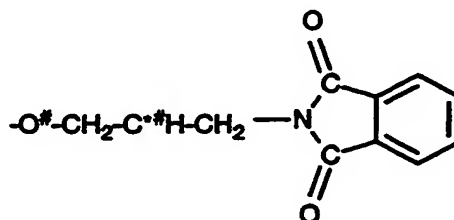
(IVC)

where:

(A) X_2 is as defined above;

(3) an (S)-phthalimide epoxide of the formula (IVD)

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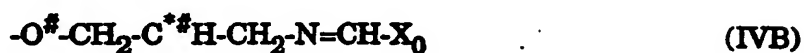
(IVD)

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where:

(A) where # indicates that the atoms marked with a (#) are bonded to each other resulting in the formation of a ring;

(4) an (S)-imine of glycidylamine of the formula (IVB)



(IVB)

25 where where X_0 and # are as defined above.

13. An (S)-compound according to claim 12 where X_0 is - ϕ or o-hydroxyphenyl and X_2 is -Cl.

30 14. An (S)-compound according to claim 12 which is
(S)-1-benzalimino-3-chloro-2-propanol and
(S)-1-phthalimido-3-chloro-2-propanol.

15. An (S)-intermediate of the formula (XV)

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(XV)

where:

(I) R_{oxa} is phenyl substituted with one -F and one substituted amino group;

(II) R_N is C_1 - C_5 alkyl;

(III) X_2 is:

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(A) -Cl,

(B) -Br,

(C) $p\text{-CH}_3\text{-}\phi\text{-SO}_2\text{-}$,

(D) $m\text{-NO}_2\text{-}\phi\text{-SO}_2\text{-}$.

10 16. An (S)-intermediate according to claim 15 where R_{oxa} is:

3-fluoro-4-[4-(benzyloxycarbonyl)-1-piperazinyl]phenyl,

3-fluoro-4-(4-morpholinyl)phenyl and

3-fluoro-4-(4-hydroxyacetyl)piperazinyl]phenyl.

15 17. An (S)-intermediate according to claim 15 where R_N is C_1 alkyl.

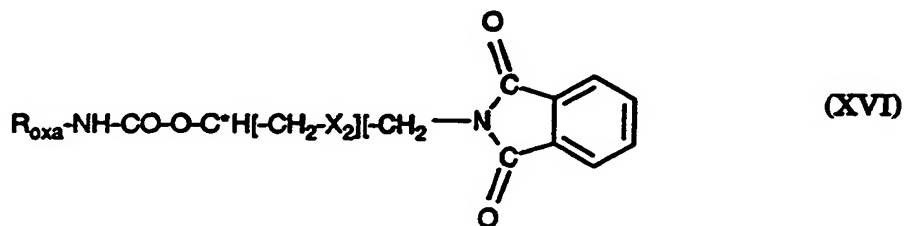
18. An (S)-intermediate according to claim 15 where X_2 is -Cl.

19. An (S)-intermediate according to claim 15 where the intermediate is

20 (S)-N-carbo(1'-acetamido-3'-chloro-2'-propoxy)-3-fluoro-4-morpholinylanilin .

20. An (S)-oxazolidinone phthalamide intermediate of the formula (XVI)

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where:

(I) R_{oxa} is phenyl substituted with one -F and one substituted amino group;

(II) X_2 is:

(A) -Cl,

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(B) -Br,

(C) $p\text{-CH}_3\text{-}\phi\text{-SO}_2\text{-}$,

(D) $m\text{-NO}_2\text{-}\phi\text{-SO}_2\text{-}$.

21. An oxazolidinone phthalamide intermediate (XVI) according to claim 21 where R_{oxa} is:

5 3-fluoro-4-[4-(benzyloxycarbonyl)-1-piperazinyl]phenyl,
 3-fluoro-4-(4-morpholinyl)phenyl and
 3-fluoro-4-(4-hydroxyacetyl)piperazinyl]phenyl.

22. An oxazolidinone phthalamide intermediate (XVI) according to claim 21 where
10 X₂ is -Cl.

23. A process for the preparation of a (S)-3-carbon amino alcohol of the formula (V)

$$15 \quad X_2-CH_2-C^+H(OH)-CH_2-NH_3^+ \quad (V)$$

where X_2 is:

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(A) -Cl,
(B) -Br,
(C) $p\text{-CH}_3\text{-}\phi\text{-SO}_2\text{-}$,
(D) $m\text{-NO}_2\text{-}\phi\text{-SO}_2\text{-}$ which comprises:
(1) contacting a non-nitrogen adduct of formula (I)

$$\text{O}=\text{CH}-\text{X}_0 \quad - \quad \cdot \quad (\text{I})$$

25 . where X_0 is:

30 (A) $-\phi$,
(B) *o*-hydroxyphenyl,
(C) *o*-methoxyphenyl,
(D) *p*-methoxyphenyl;

with aqueous ammonia (II) in the presence of an (S)-protected-epoxide of formula (III)

$$X_2-CH_2-C^{\#}H-CH_2-O^{\#}. \quad (III)$$

where:

(I) # indicates that the atoms marked with a (#) are bonded to each other resulting in the formation of a ring;

(II) X_2 is as defined above,

(2) contacting the reaction mixture of step (1) with acid.

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24. A process for the preparation of an (S)-3-carbon amino alcohol (V) according to claim 23 where X_2 is -Cl.

25. A process for the preparation of a (S)-3-carbon amino alcohol (V) according to claim 23 where the 3-carbon amino alcohol (V) is (S)-1-amino-3-chloro-2-propanol hydrochloride.

26. A process for the preparation of an (S)-3-carbon amino alcohol of the formula (V)



where:

(I) X_2 is:

(A) -Cl,

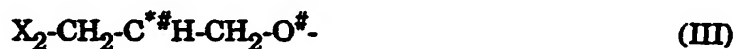
20 (B) -Br,

(C) $p-CH_3-\phi-SO_2-$,

(D) $m-NO_2-\phi-SO_2-$ which comprises:

(1) contacting phthalimide (VI)

25 with an (S)-protected-epoxide of formula (III)

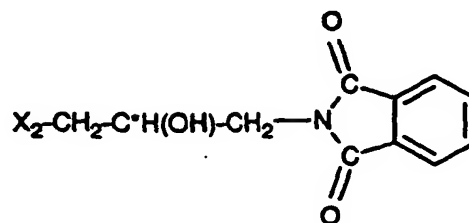


30 in the presence of potassium phthalamide in DMF or DMAC where:

(I) # indicates that the atoms marked with a (#) are bonded to each other resulting in the formation of a ring;

(II) X_2 is as defined above; to give an (S)-phthalimide alcohol of formula (IVC)

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(IVC)

where X_2 is as defined above and

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(2) contacting the product of step (1) with aqueous acid.

27. A process for the preparation of an (S)-3-carbon amino alcohol (V) according to claim 26 where X_2 is -Cl.

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28. A process for the preparation of an (S)-3-carbon amino alcohol (V) according to claim 26 where the (S)-3-carbon amino alcohol is (S)-1-amino-3-chloro-2-propanol hydrochloride.

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29. A process for the preparation of a secondary alcohol of the formula (VIII A)



where:

(I) X_2 is:

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(A) -Cl,

(B) -Br,

(C) $p\text{-CH}_3\text{-}\phi\text{-SO}_2\text{-}$,

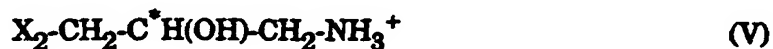
(D) $m\text{-NO}_2\text{-}\phi\text{-SO}_2\text{-}$;

(II) R_N is $C_1\text{-}C_5$ alkyl;

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which comprises:

(1) contacting an (S)-3-carbon amino alcohol of the formula (V)



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where X_2 is as defined above with an acylating agent selected from the group consisting of an acid anhydride of the formula $O(CO-R_N)$ where R_N is as defined

above or an acid halide of the formula $R_N\text{-CO-X}_4$ where X_4 is -Cl or -Br and where R_N is as defined above and a tri(alkyl)amine where alkyl is $C_1\text{-C}_5$.

30. A process for the preparation of a secondary alcohol of the formula (VIIIa)
5 according to claim 29 where the tri(alkyl)amine is triethylamine.

31. A process for the production of an (S)-oxazolidinone- $\text{CH}_2\text{-NH-CO-R}_N$ of formula (X)



where:

- (I) R_N is $C_1\text{-C}_5$ alkyl;
15 (II) R_{oxa} is phenyl substituted with one -F and one substituted amino group;
which comprises:

(1) contacting a carbamate of formula (IX)



where:

(I) X_1 is:

- (A) $C_1\text{-C}_{20}$ alkyl,
(B) $C_3\text{-C}_7$ cycloalkyl,
25 (C) ϕ - optionally substituted with one or two:
(1) $C_1\text{-C}_3$ alkyl,
(2) F-, Cl-, Br-, I-,
(D) $\text{CH}_2=\text{CH-CH}_2\text{-}$,
(E) $\text{CH}_3\text{-CH=CH-CH}_2\text{-}$,
30 (F) $(\text{CH}_3)_2\text{C=CH-CH}_2\text{-}$,
(G) $\text{CH}_2=\text{CH-}$,
(H) $\phi\text{-CH=CH-CH}_2\text{-}$,
(I) $\phi\text{-CH}_2\text{-}$ optionally substituted on ϕ - with one or two -Cl, $C_1\text{-C}_4$
alkyl, - NO_2 , -CN, - CF_3 ,
35 (J) 9-fluorenylmethyl,
(K) $(\text{Cl})_3\text{C-CH}_2\text{-}$,

(L) 2-trimethylsilylethyl,

(M) ϕ -CH₂-CH₂-,

(N) 1-adamantyl,

(O) $(\phi)_2$ CH-,

5 (P) CH₂=C-C(CH₃)₂-,

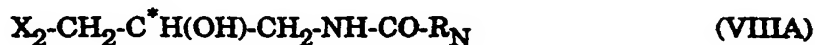
(Q) 2-furanylmethyl,

(R) isobornyl,

(S) -H;

(II) R_{oxa} is as defined above; with an oxygenated amino reagent selected from
10 the group consisting of:

(1) an (S)-secondary alcohol of the formula (VIII A)



15

where:

(I) X₂ is:

(A) -Cl,

(B) -Br,

20 (C) *p*-CH₃- ϕ -SO₂-,

(D) *m*-NO₂- ϕ -SO₂-;

(II) R_N is as defined above;

or an (S)-epoxide of the formula (VIII B)

25



where:

(I) # indicates that the atoms marked with a (#) are bonded to each other
resulting in the formation of a ring;

30 (II) R_N is as defined above;

or an (S)-ester of the formula (VIII C)



35 where:

(I) R_N and X₂ are as defined above;

in the presence of a lithium cation and a base whose conjugate acid has a pK_a of greater than about 8.

32. A process for the production of an (S)-oxazolidinone- $CH_2-NH-CO-R_N$ (X)

5 according to claim 31 where R_{oxa} is:

3-fluoro-4-[4-(benzyloxycarbonyl)-1-piperazinyl]phenyl,

3-fluoro-4-(4-morpholinyl)phenyl and

3-fluoro-4-(4-hydroxyacetyl piperazinyl)phenyl.

10 33. A process for the production of an (S)-oxazolidinone- $CH_2-NH-CO-R_N$ (X) according to claim 31 where R_N is C_1 alkyl.

34. A process for the production of an (S)-oxazolidinone- $CH_2-NH-CO-R_N$ (X) according to claim 31 where X_1 is -H.

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35. A process for the production of an (S)-oxazolidinone- $CH_2-NH-CO-R_N$ (X) according to claim 31 where X_2 is -Cl.

36. A process for the production of an (S)-oxazolidinone- $CH_2-NH-CO-R_N$ (X) according to claim 31 where the oxygenated amino reagent is a (S)-secondary alcohol (VIII A) or (S)-epoxide (VIII B).

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37. A process for the production of an (S)-oxazolidinone- $CH_2-NH-CO-R_N$ (X) according to claim 31 where the (S)-oxazolidinone- $CH_2-NH-CO-R_N$ (X) is (S)-N-[[3-(3-
25 fluoro-4-morpholinylphenyl)-2-oxo-5-oxazolidinyl]methyl]acetamide.

38. A process for the production of an (S)-oxazolidinone- $CH_2-NH-CO-R_N$ of formula (X)

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$$R_{oxa}-RING-CH_2-NH-CO-R_N \quad (X)$$

where:

(I) R_N is C_1-C_5 alkyl;

(II) R_{oxa} is phenyl substituted with one -F and on substituted amino group

35 which comprises:

(1) contacting a carbamate of formula (IX)



(IX)

where:

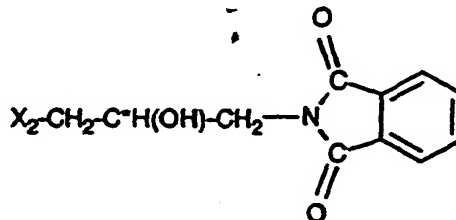
(I) X_1 is:

- 5 (A) $C_1\text{-}C_{20}$ alkyl,
 (B) $C_3\text{-}C_7$ cycloalkyl,
 (C) ϕ - optionally substituted with one or two:
 (1) $C_1\text{-}C_3$ alkyl,
 (2) F-, Cl-, Br-, I-,
 10 (D) $\text{CH}_2\text{=CH-CH}_2\text{-}$,
 (E) $\text{CH}_3\text{-CH=CH-CH}_2\text{-}$,
 (F) $(\text{CH}_3)_2\text{C=CH-CH}_2\text{-}$,
 (G) $\text{CH}_2\text{=CH-}$,
 (H) $\phi\text{-CH=CH-CH}_2\text{-}$,
 15 (I) $\phi\text{-CH}_2\text{-}$ optionally substituted on ϕ - with one or two -Cl, $C_1\text{-}C_4$
 alkyl, -NO₂, -CN, -CF₃,
 (J) 9-fluorenylmethyl,
 (K) $(\text{Cl})_3\text{C-CH}_2\text{-}$,
 (L) 2-trimethylsilylethyl,
 20 (M) $\phi\text{-CH}_2\text{-CH}_2\text{-}$,
 (N) 1-adamantyl,
 (O) $(\phi)_2\text{CH-}$,
 (P) $\text{CH=C-C(CH}_3)_2\text{-}$,
 (Q) 2-furanylmethyl,
 25 (R) isobornyl,
 (S) -H;

(II) R_{oxa} is as defined above; with a phthalimide reagent selected from the group consisting of:

(1) a phthalimide alcohol of the formula (IVC)

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(IVC)

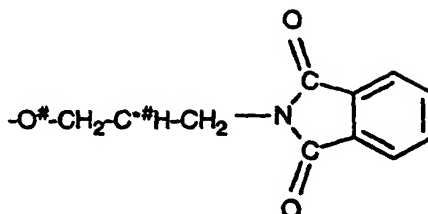
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where:

(I) X_2 is:

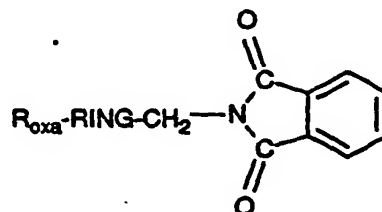
- (A) -Cl,
- (B) -Br,
- (C) $p\text{-CH}_3\text{-}\phi\text{-SO}_2\text{-}$,
- (D) $m\text{-NO}_2\text{-}\phi\text{-SO}_2\text{-}$;

(2) a phthalimide epoxide of the formula (IVD)



(IVD)

where # indicates that the atoms marked with a (#) are bonded to each other resulting in the formation of a ring to give the ring-phthalimide compound of formula (XI)



(XI)

where R_{oxa} is as defined above, in the presence of a lithium cation and a base whose conjugate acid has a pK_a of greater than about 8,

(2) contacting the product of step (1) with aqueous acid,

(3) contacting the reaction mixture of step (2) with an acid anhydride of the formula $\text{O}(\text{CO-R}_N)_2$ where R_N is as defined above or an acid halide of the formula $R_N\text{-CO-X}_4$ where X_4 is -Cl or -Br and where R_N is as defined above and a tri(alkyl)amine where alkyl is $\text{C}_1\text{-C}_5$.

39. A process for the production of an (S)-oxazolidinone- $\text{CH}_2\text{-NH-CO-R}_N$ (X) according to claim 38 where R_{oxa} is:

- 3-fluoro-4-[4-(benzyloxycarbonyl)-1-piperazinyl]phenyl,
- 3-fluoro-4-(4-morpholinyl)phenyl and
- 3-fluoro-4-(4-hydroxyacetyl piperazinyl)phenyl

40. A process for the production of an (S)-oxazolidinone-CH₂-NH-CO-R_N (X) according to claim 38 where R_N is C₁ alkyl.

41. A process for the production of an (S)-oxazolidinone-CH₂-NH-CO-R_N (X) according to claim 38 where X₁ is -H.

42. A process for the production of an (S)-oxazolidinone-CH₂-NH-CO-R_N (X) according to claim 38 where X₂ is -Cl.

43. A process for the production of an (S)-R_{oxa}-RING-CH₂-NH-CO-R_N of the formula (X)



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where:

(I) R_N is C₁-C₅ alkyl;

(II) R_{oxa} is phenyl substituted with one -F and one substituted amino group which comprises:

(1) contacting a carbamate of the formula (IX)



where: -

(I) X₁ is

(A) C₁-C₂₀ alkyl,

(B) C₃-C₇ cycloalkyl,

(C) φ- optionally substituted with one or two:

(1) C₁-C₃ alkyl,

(2) F-, Cl-, Br-, I-,

(D) CH₂=CH-CH₂-,

(E) CH₃-CH=CH-CH₂-,

(F) (CH₃)₂C=CH-CH₂-,

(G) CH₂=CH-,

(H) φ-CH=CH-CH₂-,

(I) φ-CH₂- optionally substituted on φ- with one or two -Cl, C₁-C₄

alkyl, -NO₂, -CN, -CF₃,

(J) 9-fluorenylmethyl,

(K) (Cl)₃C-CH₂-,

(L) 2-trimethylsilylethyl,

5 (M) ϕ -CH₂-CH₂-,

(N) 1-adamantyl,

(O) (ϕ)₂CH-,

(P) CH₂=C-C(CH₃)₂-,

(Q) 2-furanylmethyl,

10 (R) isobornyl,

(S) -H;

(II) R_{oxa} is as defined above; with a compound selected from the group consisting of a (S)-protected alcohol of the formula (IVA)



where:

(I) X₀ is:

(A) - ϕ ,

20 (B) o-hydroxyphenyl,

(C) o-methoxyphenyl,

(D) p-methoxyphenyl;

(II) X₂ is:

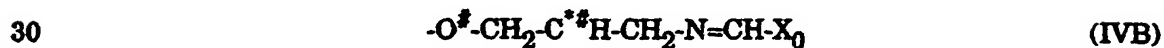
(A) -Cl,

25 (B) -Br,

(C) p-CH₃- ϕ -SO₂-,

(D) m-NO₂- ϕ -SO₂-;

and a (S)-3-carbon protected epoxide of the formula (IVB)



where:

(I) # indicates that the atoms marked with a (#) are bonded to each other resulting in the formation of a ring,

35 (II) X₀ is as defined above in the presence of a lithium cation and a base whose conjugate acid has a pK_a of greater than about 8 to produce a (S)-protected

oxazolidinone of the formula (XII)



where X_0 and R_{oxa} are as defined above;

- 5 (2) contacting the reaction mixture of step (1) with aqueous acid to produce an (S)-oxazolidinone free amine of the formula (XIII) and



- 10 (3) contacting the product of step (2) with an acylating agent selected from the group consisting of an acid anhydride of the formula $O(\text{CO-R}_N)_2$ where R_N is as defined above or an acid halide of the formula $R_N\text{-CO-X}_4$ where X_4 is -Cl or -Br and where R_N is as defined above and a tri(alkyl)amine where alkyl is $C_1\text{-C}_5$ where R_{oxa} is as defined above.

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44. A process for the production of an (S)- $R_{\text{oxa}}\text{-RING-CH}_2\text{-NH-CO-R}_N$ (X) according to claim 43 where R_{oxa} is:

3-fluoro-4-[4-(benzyloxycarbonyl)-1-piperazinyl]phenyl,

3-fluoro-4-(4-morpholinyl)phenyl and

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3-fluoro-4-(4-hydroxyacetyl)piperazinyl)phenyl.

45. A process for the production of an (S)- $R_{\text{oxa}}\text{-RING-CH}_2\text{-NH-CO-R}_N$ (X) according to claim 43 where R_N is C_1 alkyl.

25 46. A process for the production of an (S)- $R_{\text{oxa}}\text{-RING-CH}_2\text{-NH-CO-R}_N$ (X) according to claim 43 where X_0 is - ϕ or o-hydroxyphenyl.

47. A process for the production of an (S)- $R_{\text{oxa}}\text{-RING-CH}_2\text{-NH-CO-R}_N$ (X) according to claim 43 where X_1 is -H.

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48. A process for the production of an (S)- $R_{\text{oxa}}\text{-RING-CH}_2\text{-NH-CO-R}_N$ (X) according to claim 43 where X_2 is -Cl.

49. A process for the production of an (S)- $R_{\text{oxa}}\text{-RING-CH}_2\text{-NH-CO-R}_N$ of the
35 formula (X)



(X)

where:

(I) R_N is $C_1\text{-}C_5$ alkyl;

5 (II) R_{oxa} is phenyl substituted with one -F and one substituted amino group which comprises:

(1) contacting a carbamate of the formula (IX)



(IX)

10

where:

(I) X_1 is:

(A) $C_1\text{-}C_{20}$ alkyl,

(B) $C_3\text{-}C_7$ cycloalkyl,

15 (C) ϕ - optionally substituted with one or two:

(1) $C_1\text{-}C_3$ alkyl,

(2) F-, Cl-, Br-, I-,

(D) $\text{CH}_2\text{=CH-CH}_2\text{-}$,

(E) $\text{CH}_3\text{-CH=CH-CH}_2\text{-}$,

20 (F) $(\text{CH}_3)_2\text{C=CH-CH}_2\text{-}$,

(G) $\text{CH}_2\text{=CH-}$,

(H) $\phi\text{-CH=CH-CH}_2\text{-}$,

(I) $\phi\text{-CH}_2\text{-}$ optionally substituted on ϕ - with one or two -Cl, $C_1\text{-}C_4$ alkyl, -NO₂, -CN, -CF₃,

25 (J) 9-fluorenylmethyl,

(K) $(\text{Cl})_3\text{C-CH}_2\text{-}$,

(L) 2-trimethylsilylethyl,

(M) $\phi\text{-CH}_2\text{-CH}_2\text{-}$,

(N) 1-adamantyl,

30 (O) $(\phi)_2\text{CH-}$,

(P) $\text{CH}\equiv\text{C-C}(\text{CH}_3)_2\text{-}$

(Q) 2-furanylmethyl,

(R) isobornyl,

(S) -H;

35 (II) R_{oxa} is as defined above; with an (S)-3-carbon amino alcohol (V) where X_2 is as defined above in the presence of a lithium cation and a base whose conjugate

acid has a pK_a of greater than about 8 to produce an (S)-oxazolidinone free amine of the formula (XIII)

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10 where R_{oxa} is as defined above, and

(2) acylating the (S)-oxazolidinone free amine (XIII) with an acylating agent selected from the group consisting of an acid anhydride of the formula $O(\text{CO-R}_N)_2$ where R_N is as defined above or an acid halide of the formula $R_N\text{-CO-X}_4$ where X_4 is -Cl or -Br and where R_N is as defined above and a tri(alkyl)amine where alkyl is
15 $C_1\text{-C}_5$.

50. A process for the production of an (S)- $R_{\text{oxa}}\text{-RING-CH}_2\text{-NH-CO-R}_N$ (X) according to claim 49 where R_{oxa} is:

20 3-fluoro-4-[4-(benzyloxycarbonyl)-1-piperazinyl]phenyl,
3-fluoro-4-(4-morpholinyl)phenyl and
3-fluoro-4-(4-hydroxyacetyl piperazinyl)phenyl.

51. A process for the production of an (S)- $R_{\text{oxa}}\text{-RING-CH}_2\text{-NH-CO-R}_N$ (X) according to claim 49 where R_N is C_1 alkyl.

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52. A process for the production of an (S)- $R_{\text{oxa}}\text{-RING-CH}_2\text{-NH-CO-R}_N$ (X) according to claim 49 where X_1 is -H.

53. A process for the production of an (S)- $R_{\text{oxa}}\text{-RING-CH}_2\text{-NH-CO-R}_N$ (X) according to claim 49 where X_2 is -Cl.
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